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Research Article

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Determination of UV-Vis Spectrophotometric Method of Metal Complexes Stoichiometry between Cu(II), Ca(II), Cd(II), Mg(II) and Zn(II) with Bupropion Hydrochloride

Serap Karaderi*, Müge Bakla, Caner Mazı

Depertmant of Analytical Chemistry, Faculty of Pharmacy, Marmara University-34668, Haydarpaşa, Istanbul, Turkey.

***Email:** skaraderi @ marmara.edu.tr*

ABSTRACT

In this study, simple, rapid and accurate UV-Vis spectrophotometric method was developed for the determination of complexes stoichiometry of Cu(II)-bupropion hydrochloride, Ca(II)-bupropion hydrochloride, Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride. The spectrums of the complexes formed between bupropion hydrochloride with Cu (II), Ca (II), Cd (II), Mg (II) and Zn (II) metal cations were taken in the range of 500 to 190 nm and the stoichiometry of the complexes formed between bupropion hydrochloride with Cu (II), Ca (II), Cd (II), Mg (II) and Zn (II) metal cations were determined by using the mole ratio method at maximum wavelength (λmax=252 nm). The stoichiometry of Cu(II)-bupropion hydrochloride, Ca(II)-bupropion hydrochloride, Cd(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride were calculated as 1:1, but Mg(II)-bupropion hydrochloride complex was calculated as 1:2. The recovery was found 95.0% for bupropion hydrochloride. Lambert-Beer's obeyed the concentration range of 1.40-6.91 µg/mL for bupropion hydrochloride. The LOD and LOQ were found to be 13.81 and 1.38 µg/mL for bupropion hydrochloride, respectively. The interaction between bupropion hydrochloride with Cu (II), Ca (II), Cd (II), Mg (II) and Zn (II) were investigated by applying UV-visible spectrophotometric method, and satisfactory results were obtained.

Key words: *Bupropion Hydrochloride, Metal complex, Mole ratio method, Stoichiometry.*

INTRODUCTION

Depression is one of the health problems that negatively effects the health of many people in the world. It is known that depression is mostly caused by psychiatric disorders such as stress, mood, negative life conditions and genetic factors [1, 2]. Although there are various types of depression, major depression is seen as the most common psychiatric disorder among health problems. Treatment of individuals with depressive disorder can sometimes be done using antidepressant drugs such as bupropion hydrochloride [3-6]. Chemical name is 1-propanone-1-(3chlorophenyl) - 2- [(1,1dimethylethyl) amino] hydrochloride is monocyclic phenil aminoketone derivative antidepressant agent and chemical formula is $C_{13}H_{19}CI_2NO$ [7, 8]. Bupropion hydrochloride has a unique pharmacology that inhibits noradrenaline and dopamine reuptake, potentially providing pharmacological augmentation to more common antidepressants such as selective serotonergic reuptake inhibitors (SSRI). Also, bupropion hydrochloride is a monocyclic phenyl aminocetone that is effective on humans and is trimetylated. In addition to this, it is an antidepressant that acts as norepinephrine, dopamine reuptake inhibitor and nicotine antagonist [5, 9, 10]. In the literature review, some analytical methods for bupropion hydrochloride have been identified, but no studies have been conducted on the determination of the stoichiometry of complexes between bupropion with Cu (II), Ca (II), Cd (II), Mg (II) and Zn (II).

Therefore, by using the mole ratio method, it is aimed to develop a simple and accurate UV-Visible spectrophotometric method to determine the stoichiometric ratios of the complexes formed between the Cu(II), Ca(II), Cd(II), Mg(II) and Zn(II) metal cations with bupropion hydrochloride.

EXPERIMENT

Reagents and chemicals

All other reagent used were analytical grade. Pure standard of bupropion hydrochloride was purchased from Sigma-Aldrich Chemical Co. (USA). Copper (II)nitrate trihydrate, calcium(II)nitrate tetrahydrate, cadmium (II) tetrahydrate magnesium nitrate hexahydrate, zinc(II)nitrate hexahydrate and methanol reagent were obtained from Merck Chemical (Germany).

Apparatus

This experimental study was carried out on Shimadzu UV- 2550 series spectrophotometer having double beam detector configuration. The absorption spectra of reference and test solution were carried out in a 1.0 cm quartz cell (Germany) over the range of 500 to190nm.

Preparation of standard stock solutions

Bupropion hydrochloride ($1.0x10^{-3}$ M): 0.0014 g of bupropion hydrochloride was taken in to 50 mL volumetric flask and dissolved in 25 mL ultrapure water, and the volume was made up to 50 mL ultrapure water.

$Cu(NO_3)_2.3H_2O$ ($1.0x10^{-3}$ M): Copper (II) nitrate trihydrate was prepared by dissolving 0.0121 g of copper(II)nitrate trihydrate in 50 mL ultrapure water.

$Ca(NO_3)_2.4H_2O$ ($1.0x10^{-3}$ M): Calcium(II)nitrate tetrahydrate was prepared by dissolving 0.0118 g of calcium(II) nitrate tetrahydrate in 50 mL ultrapure water.

$Cd(NO_3)_2.4H_2O$ ($1.0x10^{-3}$ M): Cadmium(II)nitrate tetrahydrate was prepared by dissolving 0.0154 g of cadmium(II) nitrate tetrahydrate in 50 mL ultrapure water.

$Mg(NO_3)_2.6H_2O$ ($1.0x10^{-3}$ M): Magnesium nitrate hexahydrate was prepared by dissolving 0.0128 g of magnesium nitrate hexahydrate in 50 mL ultrapure water.

$Zn(NO_3)_2.6H_2O$ ($1.0x10^{-3}$ M): Zinc(II)nitrate hexahydrate was prepared by dissolving 0.0149 g of zinc(II)nitrate hexahydrate in 50 mL ultrapure water.

METHOD

Selection of analytical wavelength of bupropion hydrochloride

For selection of analytical wavelength, the working test solution of bupropion hydrochloride ($5x10^{-5}$ M) was scanned between 500 to 190 nm. The overlay spectrum of bupropion hydrochloride was recorded.

Selection of analytical wavelength of Cu(II)-bupropion hydrochloride and Ca(II)-bupropion hydrochloride

A number of test solutions were made by mixing different volumes of $5x10^{-5}$ M solution of each of the copper (II)nitrate trihydrate and $5x10^{-5}$ M of bupropion hydrochloride. The absorbance was scanned between 500 to 190 nm to determine their maximum wavelength using UV-2550 double-beam UV-visible spectrophotometer. The wavelength of the maximum absorbance and spectrums were recorded.

Selection of analytical wavelength of Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride

Similarly, the absorbance of working test solutions of Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride complexes were scanned between 500 to 190 nm to determine their maximum wavelengths. The maximum wavelength and spectrums for Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride complexes were recorded.

Determination of complex stoichiometry

The stoichiometries of Cu(II)-bupropion hydrochloride, Ca(II)-bupropion hydrochloride, Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride complexes were determined by using mole ratio method. To determine the Cu (II) -bupropion hydrochloride complex, a number of solutions were prepared such that the ratio of copper to bupropion hydrochloride was between 0-2.5, and the absorbance of these solutions was measured on UV spectrophotometer at the determined maximum wavelength.

Then, a graphic was drawn using the values between ligand-metal mole ratio with absorbance. Similar operations were carried out in the same manner in other metal ions.

VALIDATION PARAMETERS

Linearity and calibration curve

For linearity and calibration curve, the working solutions were prepared at 1.4, 2.76, 4.14, 5.52 and 6.91 µg/mL concentrations, respectively. The absorption spectrums of solutions were scanned on spectrophotometer in the UV range of 500 to 190 nm, and their absorbance was recorded. The calibration curve between absorbance and concentration was drawn.

Precision

Intraday and interday variations were determined by analyzing four different solutions (2.07, 3.45, 4.83 and 6.21 µg/mL) of bupropion hydrochloride within the same day and three different days over a period of week. The statistical parameters such as relative standard deviation (RSD%) and relative error (% RE) were calculated using the results obtained.

Accuracy

Accuracy of the analytical method was assessed by percentage recovery experiment performed at one level equal to 100. The known amount of standard bupropion hydrochloride solution was added to the sample solution; absorbances were recorded and reanalyzed by the proposed method. The % recovery was calculated by using the following formula:

n (mg) = C (mole/liter) x(molecular weight) (50,0 mL/1 tablet) x (dilution factor) =…… mg/ 1 tablet

% Recovery = (Found amounts of bupropion hydrochloride) / (Known amounts of bupropion hydrochloride) x 100.

The results of recovery studies are shown in Table 3.

LOD and LOQ

Limit of quantification (LOQ) and limit of detection (LOD) were calculated using the following formula: LOD=C+3s and LOQ=C+10s (C: concentration, s: standard deviation).

RESULTS AND DISCUSSION

The proposed method was based on spectrophotometric and mole ratio method determination of bupropion hydrochloride with metal complexes in UV area using the ultrapure water as a solvent. The absorption spectrums of bupropion hydrochloride, Cu(II)-bupropion hydrochloride, Ca(II)-bupropion hydrochloride, Cd(II)-bupropion hydrochloride, Mg(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride were found in the range of 500 to 190 nm. Ligand-metal complex formations were determined at a maximum wavelength of 250 nm. The curves between the absorbance and the wavelength have been shown in figures 1, 2, 3, 4, 5 and 6.

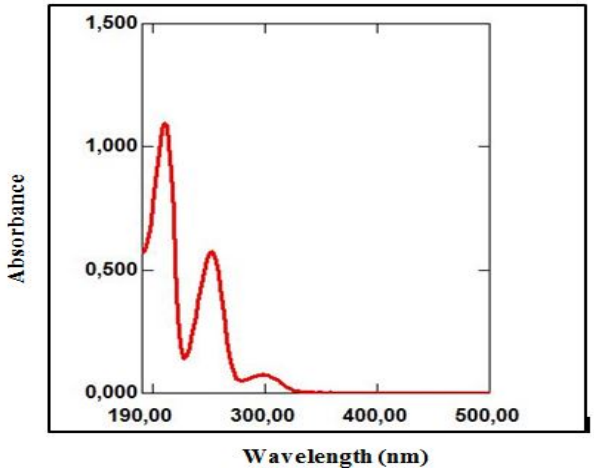

Fig. 1. The spectra of bupropion hydrochloride ($5x10^{-5}$ M)

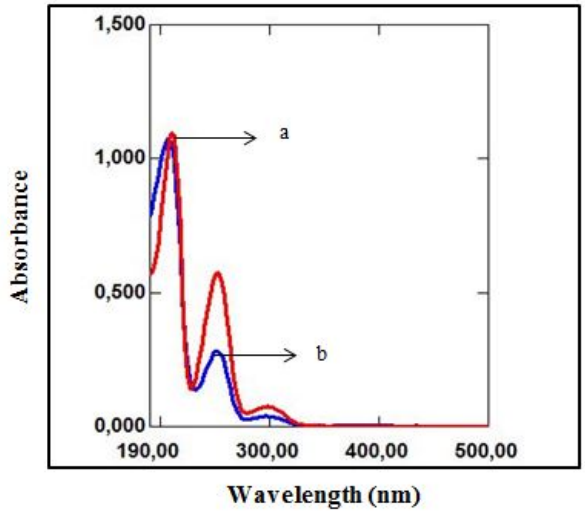

Fig. 2. a) Bupropion hydrochloride ($5x10^{-5}$ M), b) Mixture of bupropion hydrochloride-Cu (II) ($5x10^{-5}$ M) spectrums

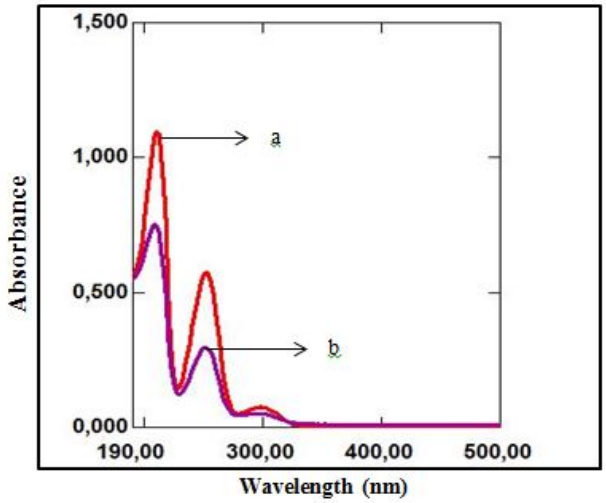

Fig. 3. a) Bupropion hydrochloride ($5x10^{-5}$ M), b) Mixture of bupropion hydrochloride-Ca (II) ($5x10^{-5}$ M) spectrums

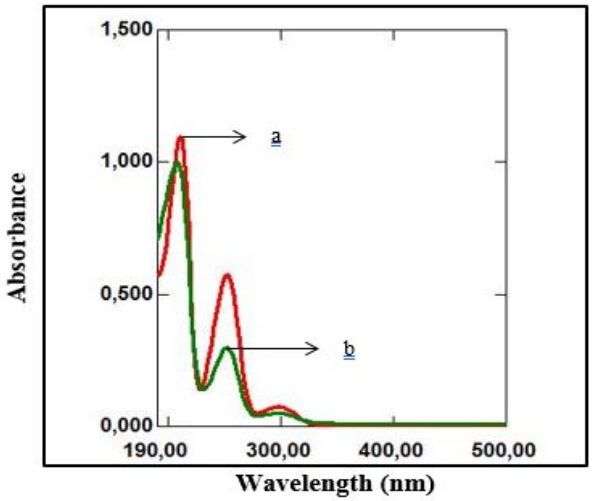

Fig. 4. a) Bupropion hydrochloride ($5x10^{-5}$ M), b) Mixture of bupropion hydrochloride-Cd (II) ($5x10^{-5}$ M) spectrums

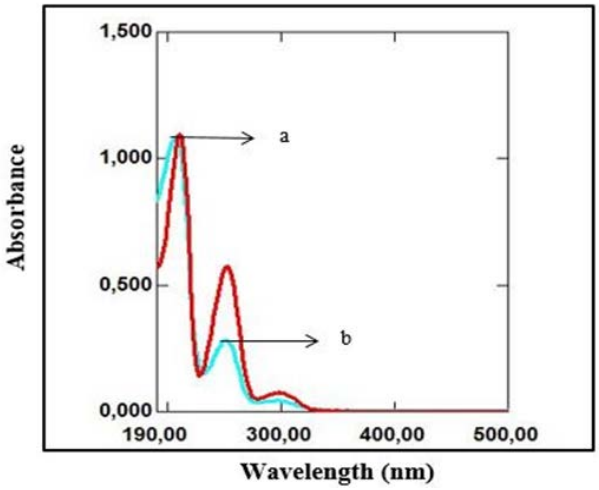

Fig. 5. a) Bupropion hydrochloride ($5x10^{-5}$ M), b) Mixture of bupropion hydrochloride-Mg (II) ($5x10^{-5}$ M) spectrums

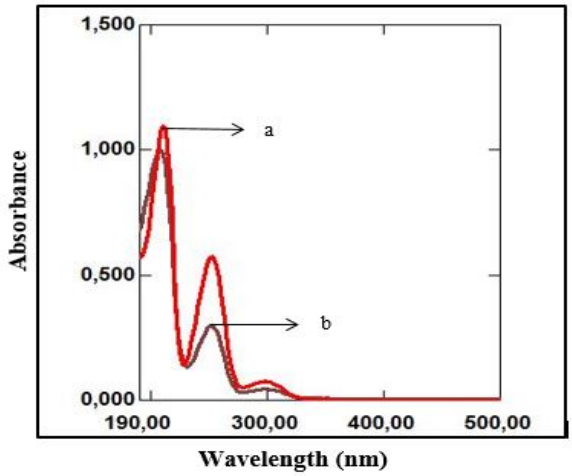

Fig. 6. a) Bupropion hydrochloride ($5x10^{-5}$ M), b) Mixture of bupropion hydrochloride-Zn(II) ($5x10^{-5}$ M) spectrums

Lambert-Beer obeyed the concentration range of 1.40-6.91 µg/mL for bupropion hydrochloride (Fig. 7 and 8). The correlation coefficient (r^2) value was found 0.9943 which showed that the absorbance of the drug was linear with concentration. The visual characteristics such as linearity range, standard deviation on intercept and slope, correlation coefficient and regression linear equation were calculated, and have been summarized in Table 1.

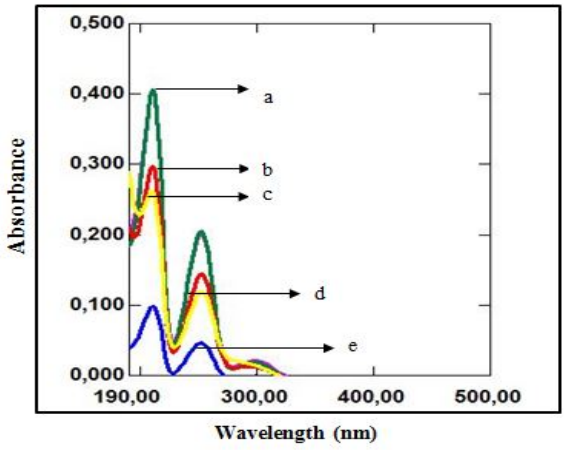

Fig. 7. Absorption spectras of five different concentrations (1.4-6.91 µg/mL) of bupropion hydrochloride

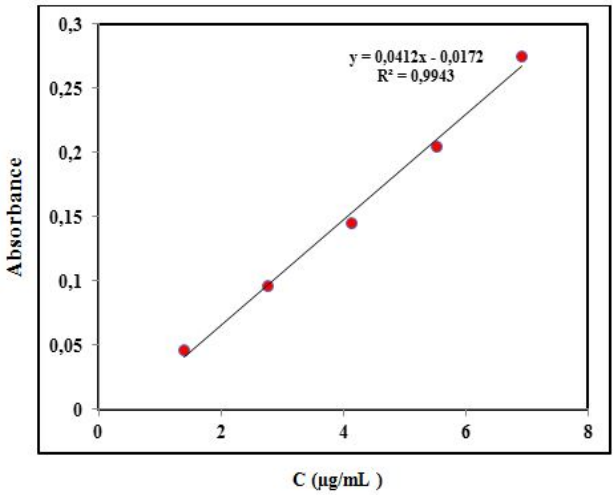

Fig. 8. Linearity plot of bupropion hydrochloride

Table 1. The statistical results of bupropion hydrochloride's calibration curve

Statistical parameters	Result
Wavelength	210 nm 252 nm 298 nm
Linearity range	1.4-6.91 µg/mL
Regression linear equation	y=0.0412x-0.0172
r^2: Correlation coefficient	0.9943
S_a: Standard deviation on intercept	0.16
S_b: Standard deviation on slope	0.017

The LOD and LOQ were found to be 13.8 µg/mL and 1.38 µg/mL for bupropion hydrochloride, respectively. The percentage relative error (RE %) and relative standard deviation (RSD %) were calculated according to the result of intraday and interday precision measurements and have been summarized in Table 2.

Table 2. Intraday and interday precision measurements results

Intraday measurement values					Interday measurement values			
Taken µg/mL	**Found µg/mL**	**x̄±s µg/mL**	**RE %**	**RSD %**	**Found µg/mL**	**x̄±s µg/mL**	**RE %**	**RSD %**
2.07	1.9 2.0 2.17	2.02±0.006	-2.42	0.30	2.09 2.07 1.95	2.04±0.003	-1.45	0.15
3.45	3.40 3.48 3.50	3.46±0.003	0.29	0.09	3.48 3.31 3.43	3.41±0.004	-1.16	0.12
4.83	4.76 4.81 4.71	4.76±0.002	-1.45	0.04	4.81 4.79 4.79	4.79±0.003	-0.83	0.06
6.21	5.98 5.85 6.34	6.10±0.010	-1.77	0.16	6.12 6.02 6.17	6.10±0.003	-1.77	0.05
x̄: Mean, s: Standard deviation, RE: Relative error, RSD: Relative standard deviation								

The recovery was found 95.0 % for bupropion hydrochloride. The result of recovery study has been shown in table 3.

Table 3. Recovery study of bupropion hydrochloride

100%	Known amounts of bupropion hydrochloride (mg)	Found amounts of bupropion hydrochloride (mg)	Recovery %
1	20.6	19.27	93.54
2	20.6	19.52	94.76
3	20.6	19.88	96.5
The mean recovery %	20.6	19.56	95.0

The stoichiometry of Cu(II)-bupropion hydrochloride, Ca(II)-bupropion hydrochloride, Cd(II)-bupropion hydrochloride and Zn(II)-bupropion hydrochloride complexes were calculated as 1:1, but Mg(II)-bupropion hydrochloride complex was calculated as 1:2. (Fig.9, fig. 10, fig. 11, fig. 12 and fig. 13).

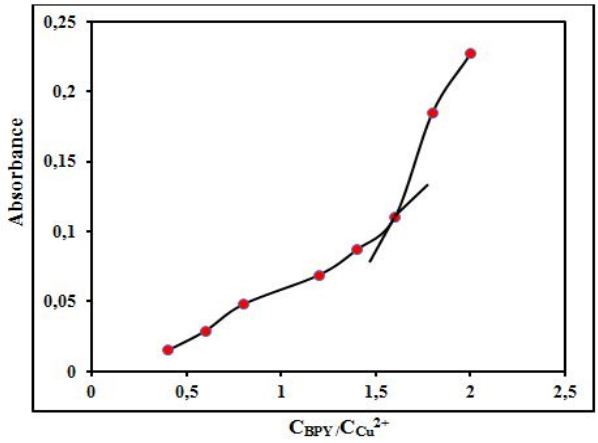

Fig. 9. Determination of composition of Cu(II)-bupropion hydrochloride complex by mole ratio method

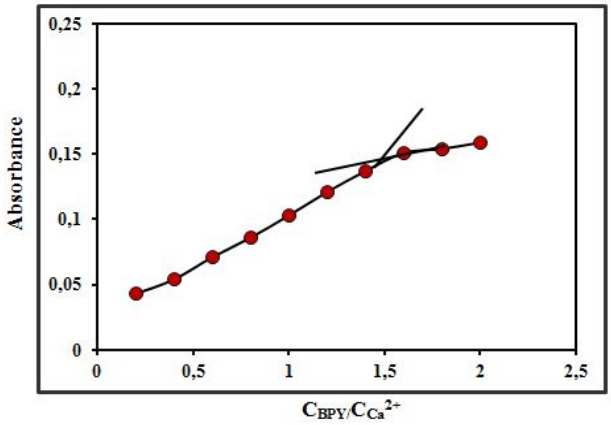

Fig. 10. Determination of composition of Ca(II)-bupropion hydrochloride complex by mole ratio method

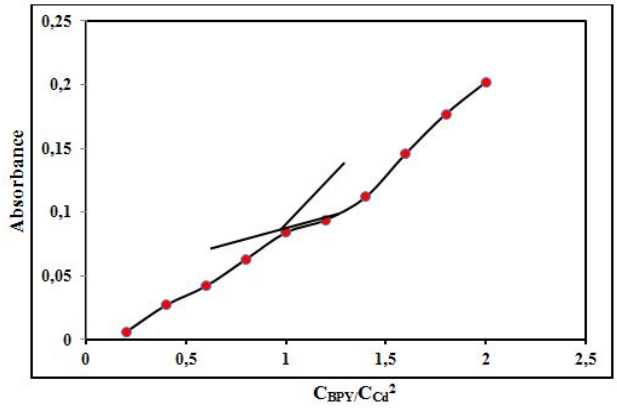

Fig. 11. Determination of composition of Cd(II)-bupropion hydrochloride complex by mole ratio method

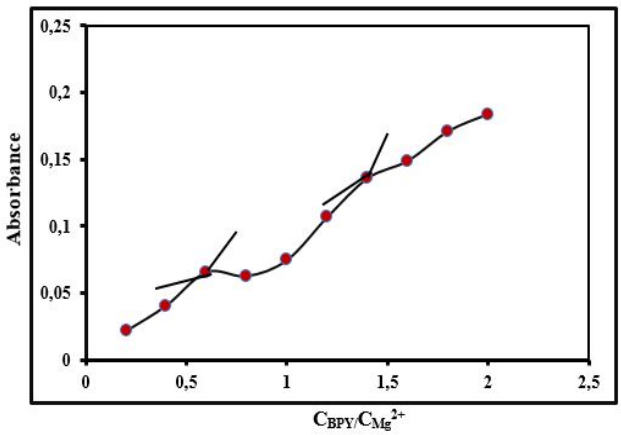

Fig. 12. Determination of composition of Mg(II)-bupropion hydrochloride complex by mole ratio method

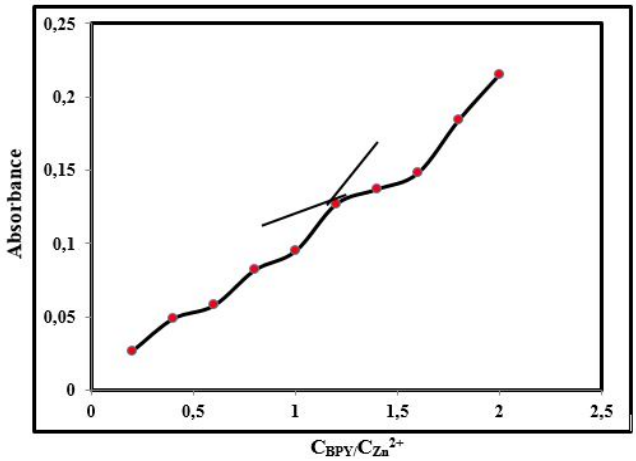

Fig 13. Determination of composition of Zn (II)-bupropion hydrochloride complex by mole ratio method

CONCLUSIONS

For all the values, low relative errors (RE< ±15 %), high correlation coefficient (r^2=0.9943) and high percentage recovery (95.0%) showed the high linear relationship between the predicted and actual concentrations. The values of % RSD was less than two (< 2%), with no significant difference in values for intra-day and inter-day precision, indicate the method's reproducibility with high precision. İn addition, the RSD values obtained from the spectrophotomeric and chromotographic studies on bupropion hydrochloride in the literature and the values obtained in our study were found to be statistically lower than the limit value (RSD <2%) in the literature (Table 2). The lack of statistically significant difference between the values of the validation parameter (precision, accuracy, linearity, LOD and LOQ) for bupropion hydrochloride proved the system's suitability for the developed UV-Vis spectrophotometric method. Literature information about complexes occurring between bupropion hydrochloride and metal cations was obtained. We think that this information will contribute to the literature. As a result, the precision of the analytical method was further substantiating. The proposed spectrophotometric method was found to be simple, rapid and accurate.

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